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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,964	11/05/2001	Carlos Miguel Carcagno	1909.0030002	5291

7590 06/01/2004

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EXAMINER	
LEITH, PATRICIA A	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,964	CARCAGNO ET AL.	
	Examiner	Art Unit	
	Patricia Leith	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-16* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are pending in the application.

The Examiner originally examined claims 1-12 on the merits. However, this was an inadvertent error since Applicant's elected claims 13-16 in the response filed 9/17/03. The Examiner regrets any confusion caused. However, this Office Action is being issued as a non-final action. Further, because claims 1-12 were originally examined, these claims have been rejoined with claims 13-16 for examination purposes, and hence, the original restriction requirement is hereby removed.

Claims 1-16 were examined on the merits.

Claim Objections

Claims 1-12 are objected to because of the following informalities:

Claim 1 states '..comprising by a combination...'. It is thought that Applicants intend for this to read 'comprising a combination'. This appears to be a typographical error.

Claims 1-12 state steps, wherein the steps (x, y and z for example) are recited as either x) or (x); or y) or (y). In order for the claims to possess consistency, Applicants are asked to either recite the steps in x) or in (x) format. It is suggested, that since claim 1 recites (x), that all of the proceeding claims also follow this format.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the term 'employed'. This term lacks clear antecedent basis in the preceding claim because claim 5 did not recite the term 'employ', but recited the word 'using'. Correction is necessary.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of purifying recombinant human erythropoietin from cell culture supernatants comprising recombinant erythropoietin by the method of claim 2, does not reasonably provide enablement for a method for purifying recombinant human erythropoietin from any cell culture supernatant via any combination of the claimed purification steps. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in

determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Wands now requires that one consider the number of working examples presented in the instant specification. It is noted that there in not a single example in the instant specification, working or prophetic, wherein any other purification sequence besides the sequence recited in claim 2, would produce a purified EPO with the characteristics as described in the Instant specification. Since there are **no** working examples, then one must consider the guidance provided by the instant specification and the prior art of record.

The art of protein purification is highly unpredictable, and often requires tedious trial and error protocols in order to sufficiently purify the protein within reasonable purity levels without damaging the protein, and without losing substantial yield. Erythropoietin is a protein which is documented in the art as being difficult to purify: "The differentiation of mammalian and avian red blood cells from comminuted progenitors within the marrow [1], spleen[2], and fetal liver [3] requires exposure to the hematopoietic growth factor, erythropoietin. ***However, the limited availability of erythropoietin and the difficulty associated with its purification have hindered***

studies of this glycoprotein hormone and its receptor" (emphasis added) (Wojchowski et al.).

To argue that one can make material embodiments of the invention and then test for those that work in the manner disclosed or that the instant claims only encompass the working embodiments is judicially unsound. Unless one has a **reasonable expectation** that any one material embodiment of the claimed invention would be more likely than not to function in the manner disclosed or the instant specification provides sufficient guidance to permit one to identify those embodiments which are **more likely to work that not** without actually making and testing them then the instant application does not support the breadth of the claims. In the instant case, the skilled artisan would not have a reasonable expectation that *any* combination of chromatographic methods would purify EPO to have the characteristics as taught in the Instant specification (i.e., purity level, yield). On the contrary, the skilled artisan would need to perform undue experimentation in order to validate the scope of the claimed invention. This experimentation would be undue, considering that the skilled artisan would not have a reasonable expectation of success. The skilled artisan would understand that purification of EPO is unpredictable, and that protein purification as a whole requires difficult and tedious experimentation. Ultimately, the skilled artisan would realize that one could not reasonably predict the yield and/or purity level of EPO eluting from each respective chromatographic step until the experiment has actually been performed. It

is further noted that in addition to the experimentation being undue, this experimentation would be an undue cost burden on the artisan because column resins are expensive.

Additionally, the skilled artisan would not have any reasonable expectation that EPO could be purified from any cell culture. For example, the skilled artisan would reasonably expect that yeast cell culture would not contain EPO. The Specification has not taught the skilled artisan how to purify EPO from cell cultures such as yeast cells, and therefore the skilled artisan would need to perform undue experimentation in order to ascertain how to use the method commensurate in scope with the claimed invention.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, *he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112*; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity,

scope of enablement varies inversely with degree of unpredictability of factors involved."

(Emphasis added)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosen (WO 92/06116). Claims 13-16 are drawn to a substantially pure erythropoietin produced according to the method of Claim 1.

Rosen (WO 92/06116) disclosed erythropoietin with Applicant's SEQ ID NO 1 as SEQ ID NO 3 (p.32).

It is noted that: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The ***patentability of a product does not depend on its method of production***. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a

different process." (emphasis added) *In re Thorpe*, 777F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

It is clear from Rosen that the erythropoietin of SEQ ID NO 1 is known in the art. Although the erythropoietin may have been obtained by another method distinct from that stated in claim 1, it is never the less the same product.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

It is deemed that since Rosen provided sequence data of the erythropoietin, that it was purified erythropoietin. It is noted however, that the percentage of purity does not materially change the physical characteristics of erythropoietin for patentability purposes. It is further noted that wherein claim 15 recites isoelectric points is merely an inherent property of the erythropoietin SEQ ID NO 3 as disclosed by Rosen. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art

teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990)

Allowable Subject Matter

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No Claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia Leith
Primary Examiner
Art Unit 1654

05/27/04

PATRICIA LEITH
PRIMARY EXAMINER